General

Guideline Title

Osteoporosis: prevention and treatment.

Bibliographic Source(s)

University of Michigan Health System. Osteoporosis: prevention and treatment. Ann Arbor (MI): University of Michigan Health System; 2011 Dec. 16 p. [13 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Osteoporosis: prevention and treatment. Ann Arbor (MI): University of Michigan Health System; 2010 Jul. 15 p.

Recommendations

Major Recommendations

Note from the University of Michigan Health System (UMHS) and the National Guideline Clearinghouse (NGC): The following guidance was current as of December 2011. Because UMHS occasionally releases minor revisions to its guidance based on new information, users may wish to consult the original guideline document for the most current version.

Note from NGC: The following key points summarize the content of the guideline. Refer to the full text of the original guideline document for detailed information on diagnosis, risk assessment, screening, prevention, treatment, and medications.

The strength of recommendation (I-III) and levels of evidence (A-D) are defined at the end of the "Major Recommendations" field.

Definitions

Bone mineral density [BMD] correlates with skeletal strength and fracture risk.

Dual-energy X-ray absorptiometry [DXA] measures BMD.

A DXA *T-score* is the number of standard deviations from mean BMD in young adults.

Osteoporosis is defined as a DXA T-score ≤-2.5, *osteopenia* as >-2.5 but <-1.0 (see Table 1 in the original guideline document).

General Clinical Relevance

Fractures related to osteoporosis are common and have high morbidity *[C]*.

Glucocorticoids can cause significant bone loss, particularly during the first 6-12 months of use *[B]*.

Prevention

Across life span: appropriate calcium and vitamin D (see Table 9 in the original guideline document) and weight bearing exercise *[ID]*.

Risk Assessment and Diagnosis

Assess all adults, men and women, for clinical risk factors for osteoporotic fracture (see Tables 2 and 3 in the original guideline document) *[IC]*:

- Postmenopausal woman with one or more of the following:
  - Age ≥65 years
  - Current smoking
  - Low body weight (BMI <20)
  - Frailty (e.g., unable to rise from chair unassisted)
  - Personal history of fracture without substantial trauma
  - Hip, wrist, or spine fracture without substantial trauma in 1st degree relative ≥50
- Chronic glucocorticoid use (prednisone ≥5 mg daily, or equivalent, for ≥3 months)
- Organ transplant or pending transplant
- Risk for falling (see Table 4 in the original guideline document)
- Other associated medical conditions (see Table 2 in the original guideline document) and medications (see Table 3 in the original guideline document)

Order DXA *[IA]* based on clinical risk factors and potential impact of results on management (see Table 5 in the original guideline document).

For women under 65, FRAX (World Health Organization Fracture Risk Assessment Tool; http://www.shef.ac.uk/FRAX/) can be used to assess need for screening DXA.

DXA is indicated for women with 10-year total fracture risk of 9.3% (equivalent to that of a healthy 65 year-old woman). In this setting, FRAX can be used without entering BMD data.

Evaluate appropriately and refer, when indicated, for secondary causes of osteoporosis (see Table 6 in the original guideline document) *[IID]*.

Treatment

For treatment-naive women, FRAX (http://www.shef.ac.uk/FRAX/) can be used to assess need for treatment.

Begin medical therapy for 10-year fracture risks of >3% at hip or >20% total fracture risk. For other patients, based on T-score and clinical risk factors (see Tables 2, 3 and 5 in the original guideline document), begin medical therapy for:

- Prior osteoporosis-related fracture, or T-score <-2.5 *[IA]*.
- T-score ≤-1 and (a) glucocorticoid use or (b) pending or post-transplant, especially if on steroids or (c) postmenopausal woman at high risk *[IA])*.
- T-score between -2 and -2.5 in postmenopausal woman *[IA]* and patients with appropriate risk factors.

When starting glucocorticoids, consider medical therapy to prevent or treat osteoporosis *[IIA]*.

Base medical therapy (see Tables 7 and 9 in the original guideline document) on clinical benefits and potential risks *[I]*:

- In post-menopausal women with osteoporosis:
  - Alendronate, denosumab, estrogen, risedronate, and zoledronic acid reduce hip and vertebral fracture risk *[A]*.
  - Ibandronate, raloxifene, teriparatide, and calcitonin reduce vertebral fracture risk *[IA]*
- In men with osteoporosis, alendronate reduces vertebral fracture risk *[A]* (probably class effect *[D])*.
- If on a glucocorticoid, use bisphosphonates (oral or intravenous [IV]) *[A]*. For alternative treatments, consider teriparatide or denosumab *[A]*.

Follow-up

Repeat DXA based on patient's situation (see Tables 5 and 8 in the original guideline document) *[IC-D]*. Consider not repeating DXA on patients

with moderate bone loss who are fracture-free on medical therapy *[IIC]*.

For most persons, ≥2 years between DXAs provides the most meaningful information *[B]*.

Early in glucocorticoid use and/or after transplantation consider repeating DXA in 6-12 months *[IB]*.

Definitions:

Level of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

Grade of Recommendation

I. Generally should be performed
II. May be reasonable to perform
III. Generally should not be performed

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Osteoporosis in postmenopausal women
- Secondary osteoporosis related to long-term glucocorticoid use, organ transplant, or other medical conditions

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Obstetrics and Gynecology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To decrease osteoporotic fractures and their associated morbidity and mortality

Target Population

Postmenopausal women and persons at risk for secondary osteoporosis related to long-term glucocorticoid use, organ transplant, or other medical conditions

Interventions and Practices Considered

Prevention

1. Weight bearing exercise
2. Adequate dietary calcium and vitamin D
3. Regular physical activity
4. Avoiding heavy alcohol consumption and smoking
5. Minimizing exposure to glucocorticoid therapy
6. Preventive use of bisphosphonates during glucocorticoid therapy

Risk Assessment/Diagnosis/Screening

1. Assessment of risk factors (e.g., age, smoking status, body weight, frailty, history of fracture, chronic glucocorticoid use, organ transplant status, other associated medical conditions and medications, and risk for falling)
2. Dual emission x-ray absorptiometry (DXA) measurement of bone mineral density (BMD)
3. Use of FRAX (fraction risk assessment tool) to assess for need for DXA or treatment
4. Quantitative calcaneal ultrasound devices (considered but not recommended)
5. Measurement of biochemical markers of bone resorption (considered but not recommended)
6. Evaluation and referral for secondary causes of osteoporosis

Treatment/Management

1. Non-pharmacologic therapies
    - Weight bearing exercises
    - Fall prevention measures
    - Anatomically designed hip protectors
2. Pharmacologic therapies
    - Calcium and vitamin D
    - Bisphosphonates (such as alendronate, risedronate, zoledronic acid, and ibandronate)
    - Denosumab

    - Parathyroid hormone (teriparatide)
    - Selective estrogen receptor modulators (SERMs) (e.g., raloxifene)
    - Estrogen and progestin (and combinations)
    - Calcitonin nasal spray
3. Other pharmacologic therapies (considered but not necessarily recommended at this time)
    - Combination therapy
    - Calcitriol
    - Tamoxifen
    - Testosterone replacement or supplement in men
    - Thiazide diuretics (e.g., hydrochlorothiazide)
    - Phytoestrogens, including isoflavones
4. Follow-up: repeat DXA measurement

Major Outcomes Considered

- Risk for osteoporosis and osteoporotic fractures
- Incidence of osteoporosis and osteoporotic fractures
- T-score
- Predictive value of diagnostic tests (DXA)
- Mortality related to osteoporotic hip fractures
- Morbidity (chronic pain, disability, deformity, depression) related to osteoporotic fractures
- Pain relief
- Medication side effects
- Incidence of falls

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The literature search for this update began with the results of the search performed for the 2002 version of this guideline. That search began with the results of a search performed by the National Osteoporosis Foundation (Osteoporosis: review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis), published in 1998 and including literature through 1996. Medline was then searched for literature from 1996 through 1999. Details of that search (similar to the update search explained below) were described in the 2000 guideline.

The search for the 2010 update of this guideline was performed on literature from 2000 through April 2007. The search was conducted prospectively using the major key words of: osteoporosis (including osteoporosis, postmenopausal); osteopenia; English language; and guidelines or controlled trials. Specific searches were performed for special risk categories (steroids, transplant, men/males/ non-Caucasian women/African-American women). For postmenopausal osteoporosis, specific searches were performed for risk factors (general risk factors, progestins, aromatase inhibitors, parathyroid), diagnostic testing (bone density scan/DXA, metabolic bone markers, bone quality, ultrasound), pharmacologic therapies (calcium, Vitamin D/calcitriol, bisphosphonates, raloxifene, calcitonin, hormone replacement therapy, teriparatide, tamoxifen/SERMS, testosterone/androgens, thiazide diuretics, HMG-coA-reductase inhibitors, phytoestrogens, strontium), non-pharmacologic strategies (exercise, fall prevention), alternative and complementary therapies (phytoestrogens, isoflavanoids), and monitoring (DXA frequency). The detailed search strategy is available upon request.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search

was supplemented with very recent (through June 2009) clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

The review of literature was assisted by the publication in December 2007 of a systematic review of treatments: Comparative Effectiveness of Treatments to Prevent Fractures in Men and Women with Low Bone Density or Osteoporosis. The Agency for Healthcare Research published this review, which examined literature from 1966 through December 2006.

The 2011 interim revision of the guideline was based on literature reviews performed for recently published national guidelines and very recently recent (through July 2011) clinical trials known to expert members of the panel. The topic of denosumab was added.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Conclusions were based on prospective randomized controlled trials (RCTs), if available, to the exclusion of other data. If RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was uses to estimate effect size. The "strength of recommendation" for key aspects of care was determined by expert opinion.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

I. Generally should be performed
II. May be reasonable to perform
III. Generally should not be performed

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Drafts of this guideline were reviewed in clinical conferences and by distribution within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, General Medicine, Geriatric Medicine, Metabolism and Endocrinology, and Obstetrics and Gynecology (Women's Health). The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Conclusions were based on prospective randomized controlled trials (RCTs), if available, to the exclusion of other data. If RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was uses to estimate effect size.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved identification of patients at high risk for osteoporosis and osteoporotic fractures
- Decreased incidence of osteoporotic fractures and associated morbidity and mortality

Potential Harms

Non-drug Therapies

Anatomically designed hip protectors. Hip protectors are often difficult to put on, and uncomfortable to wear; therefore, compliance may play a role in reducing their potential effectiveness.

Drug Therapies

- *Calcium*. Constipation is more common with calcium carbonate.
- *Vitamin D*. Vitamin D is fat-soluble, and thus toxicity can result from excess dosing.
- *Bisphosphonates*
    - Oral bisphosphonate trials have reported esophageal complications ranging from heartburn and acid reflux to esophageal ulceration and perforation, which are quite rare. The FDA is currently investigating a possible connection between esophageal cancer and oral

bisphosphonates.
    - Effects on fetal development are not known. Prolonged presence in bone of treated patients: discuss potential fetal risks if considering for women of child-bearing age.
    - Osteonecrosis of the jaw (ONJ) has emerged as a more serious complication of high dose bisphosphonate therapy. Risk of ONJ is less than 1 in 100,000 for oral bisphosphonates.
    - Bisphosphonate use has been associated with musculoskeletal pain, and this side effect has been included in the prescribing information for all drugs in this class. However, in January 2008, the U.S. Food and Drug Administration (FDA) highlighted this risk, reminding clinicians to consider bisphosphonates when evaluating patients with musculoskeletal pain.
    - Atypical femoral shaft fractures may also be associated with bisphosphonate use, and is being investigated by the FDA. These fractures tend to occur without trauma, and may be preceded by the sudden onset of thigh pain. The estimated risk of this complication is 1:10.000.
    - *Zoledronic acid* has been associated with a small increase in atrial fibrillation.
- *Denosumab* is associated with an increased risk of cellulitis, although the risk is low (<0.5%). Other infections may be more common in patients on denosumab.
- *Teriparatide*. Teriparatide was associated with an increased incidence of osteosarcoma in rats given high doses over an extended period. Given this concern, it should not be used in patients with a history of bony malignancy, or those at risk.
- *Raloxifene*. An increased risk of deep venous thrombosis and pulmonary embolism approximately the same as estrogen therapy, as well as hot flashes have been associated with raloxifene. Raloxifene is not recommended for use in premenopausal women.
- *Estrogen*. Preparations and formulations identified as 'bioidentical hormones' do not have evidence demonstrating benefit in fracture reduction, or even safety, when compared to FDA-approved sources of estrogen.
- *Calcitonin nasal spray*. Rhinitis has been observed in 5% excess compared with placebo. Caution is urged with calcitonin nasal spray in renal failure.

Contraindications

Contraindications

- Reflux without esophagitis is a relative but not an absolute contraindication of bisphosphonates.
- Bisphosphonates should be avoided if creatinine clearance is <30 to 35. Bisphosphonates should not be used in women who are, or plan to become pregnant.

Qualifying Statements

Qualifying Statements

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2002 Mar (revised 2011 Dec)

Guideline Developer(s)

University of Michigan Health System - Academic Institution

Source(s) of Funding

University of Michigan Health System

Guideline Committee

Osteoporosis Guideline Team

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Financial Disclosures/Conflicts of Interest

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member	Relationship	Company
Van Harrison, PhD	(None)	
Robert Lash, MD	(None)	
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Jane Nicholson, MD	(None)	
Lourdes Velez, MD	(None)	

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Osteoporosis: prevention and treatment. Ann Arbor (MI): University of Michigan Health System; 2010 Jul. 15 p.

Guideline Availability

Electronic copies: Available from the University of Michigan Health System Web site .

Availability of Companion Documents

Continuing Medical Education (CME) information is available from the University of Michigan Health System Web site .

Patient Resources

The following are available:

- Osteoporosis in women. Patient education handout. Ann Arbor (MI): University of Michigan Health System; 2009 Jul. Various p. Electronic copies: Available from the University of Michigan Health System (UMHS) Web site .
- Calcium and vitamin D. Patient education handout. Ann Arbor (MI): University of Michigan Health System; 2010 Aug. Various p. Electronic copies: Available from the UMHS Web site . Also available in Spanish from the UMHS Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a

licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on March 19, 2003. The information was verified by the guideline developer on April 23, 2003. This NGC summary was updated by ECRI on September 22, 2005. The updated information was verified by the guideline developer on November 1, 2005. This NGC summary was updated by ECRI Institute on October 14, 2010. This summary was updated by ECRI Institute on December 10, 2010 following the U.S. Food and Drug Administration (FDA) advisory on Bisphosphonates. This summary was updated by ECRI Institute on October 12, 2011 following the U.S. Food and Drug Administration (FDA) advisory on Reclast (zoledronic acid). This NGC summary was updated by ECRI Institute on March 23, 2012. This summary was updated by ECRI Institute on April 3, 2015 following the U.S. Food and Drug Administration advisory on Testosterone Products.

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